York), who introduced "DES Education and Research Amendments of 1992" (H.R. 4178); the companion bill was S.2837, introduced by Senator Tom Harkin (D-Iowa).

Role of p53 in Cellular Response to DNA Damage

Normally, when DNA is damaged, synthesis of new DNA is halted until the DNA is repaired. If synthesis is not halted, newly synthesized DNA may be at risk for genetic errors, which could lead to malignancies. Michael Kastan, an NIEHS grantee at Johns Hopkins University, has investigated the role of p53 in the cellular response to DNA damage. Elucidation of p53 gene expression is particularly important because it is the most commonly mutated gene in human cancer.

Kastan's laboratory has demonstrated, confirmed, and clarified the link between p53 and the arrest of the cell cycle at the G_1 phase after ionizing radiation. His laboratory has observed this phenomenon in many cell types and in several tumor cell lines. Kastan and colleagues transfected a cell line (HL-60) that had no endogenous p53 with wild-type p53. These transfected cells demonstrated G_1 arrest after irradiation. A tumor cell line was transfected with a mutant p53 gene and did not demonstrate G_1 arrest after irradiation.

Normal fibroblasts from mice in which both alleles of p53 had been disrupted were defective at this G_1 checkpoint. Kastan's laboratory is now investigating agents that affect p53 levels. Topoisomerase inhibitors induce p53, whereas base-damaging agents do not. Kastan is also studying the biochemical pathways involved in altering p53 protein levels and cell-cycle progression after DNA damage. His group has demonstrated that genes that are defective in the cancer-prone disease ataxia-telangiectasia are necessary for the induction of the p53 protein. Finally, they have shown that the gene GADD45, which is activated by growth arrest or DNA damage, is regulated by p53.

Air Pollutant Related to Genetic Damage in Poland

Frederica Perera and colleagues at Columbia University, Sweden's Center for Nutrition and Toxicology, and the Institute of Oncology in Poland have provided the clearest evidence to date of a direct link between environmental air pollutants and cancer-related genetic damage. This study, published in *Nature* and funded in part by NIEHS, broke new ground by using a sophisticated battery of biomarkers to detect potential environmental cancer risk. The researchers studied two population groups in Poland, a highly exposed group living in the town of Gliwice, Upper Silesia, characterized by high rates of cancer, and unexposed controls from Biala Podlaska, a rural province with roughly one-tenth the air pollution levels in Gliwice.

Perera and her colleagues found considerably higher levels of DNA and chromosomal damage in the exposed population compared to the controls. A doubling in the frequency of oncogene activation also occurred in the exposed group. These studies provide a molecular link between the environmental exposure and a genetic alteration relevant to cancer and reproductive risk.

Protein Identified that Protects against Lymphomas

Transgenic mice that express the human homolog of a particular protein in the thymus were protected when exposed to a known carcinogen, *N*-methyl-*N*-nitrosourea, in a study conducted under an NIEHS grant by Stanton Gerson at Case Western Reserve University. Findings of the study were published in *Science* in January 1993. In view of these findings with experimental tumors, gene therapy methods may merit consideration.

NIEHS Laboratory of Molecular Genetics Receives Award

Michael Resnick's laboratory within the NIEHS Laboratory of Molecular Genetics has received a $470,000 award from the National Center for Human Genome Research, NIH, to continue studies on the role of recombination in the instability of human DNA containing yeast artificial chromosomes (YACs) with the purpose of developing a system that has few errors.

Dr. Michael Resnick

The Human Genome Initiative is a worldwide effort to map and sequence the human genome as well as to identify and characterize sources of genetic disease. These efforts rely heavily on the use of YACs; however, as many as 50% of YACs containing human DNA have deletions, rearrangements, or noncontiguous chromosomal sequences.

Resnick's laboratory, in collaboration with Vladimer Larionov and Natasha Kouprina, visiting scientists from St. Petersburg, Russia, has been able to demonstrate that recombination is a key source of errors in cloning and maintaining human DNAs in yeast. The laboratory's work, previously supported by the Department of Energy, has led to the identification of mechanisms and genetic controls of the errors and has already elucidated some of the underlying mechanisms of recombination in eukaryotes.

Tumor-Suppressor Genes and Oncogenes

The NIEHS Laboratory of Molecular Carcinogenesis uses microcell-mediated chromosome transfer techniques to locate chromosomes containing a variety of human and rodent cancer tumor-suppressor genes. In collaboration with John Isaacs of Johns Hopkins University, the laboratory, directed by J. Carl Barrett, has shown that somatic cell hybridization of highly metastatic and nonmetastatic rat prostate cancer cells can be rendered nonmetastatic.

Because the major problems associated with prostate cancer morbidity and mortality are a consequence of its ability to aggressively spread to the bone, attempts are being made to locate the region of the human chromosome that confers metastatic ability to cancerous prostate cells. The gene has been shown to lie in a specific region (between 11p11.2-13, but not including the Wilms' tumor-1 locus). Further attempts at characterization are ongoing.

NIEHS Joins EPA and NCI in Agricultural Health Study

NIEHS has joined the Environmental Protection Agency and the National Cancer Institute in a $15-million, 10-year epidemiological study on the health of farmers, their families, and other workers who apply agricultural chemicals. Although the study will look closely at cancers, NIEHS will especially look at non-cancer disease and dysfunction, including reproductive effects, childhood and adult asthma, immunological effects, lactation, neurological outcomes, childhood development, kidney disease, and birth defects. Dale P. Sandler, NIEHS Epidemiology Branch, will lead the study at NIEHS.

Subjects for the study will be selected from farm families and agricultural workers in Iowa and North Carolina. The subjects in the Iowa cohort will be primarily white, but the North Carolina cohort will include a substantial number of nonwhites, especially African-Americans and Native Americans. The 200 households in the study will be monitored at least twice, during the growing season and off-season, and the study will evaluate environmental factors (air, water, food, soil, house dust) as well as biological samples (blood and urine).

Kenneth Olden, NIEHS director, has visited Iowa farm families to discuss environmental health concerns with those